

Hypotheses Regarding Ammonia Compounds

1. Ammonia compounds increase the amount of nicotine that transfers from the tobacco into cigarette smoke.
2. The use of ammonia compounds increases the "smoke pH".
3. Higher "smoke pH" increases the amount of nonprotonated ("free") nicotine in the smoke.
4. Nonprotonated ("free") nicotine is absorbed into the bloodstream more rapidly than protonated nicotine.
5. Nicotine when more rapidly absorbed is more addictive.

Secondary Hypothesis Regarding Ammonia Compounds

- The use of ammonia compounds increases the amount of nicotine in the gas phase which is not detected by standard methods which measure nicotine in mainstream cigarette smoke (the FTC/ISO methods).

Hypotheses Regarding Ammonia Compounds

Source

D. A. Kessler

"The Control and Manipulation of Nicotine in Cigarettes," before the Subcommittee on Health and the Environment Committee on Energy and Commerce U. S. House of Representatives June 21, 1994

C. Bates, M. Jarvis, and G. Connolly

"Tobacco Additives; Cigarette Engineering and Nicotine Addition," July 14, 1999

www.ash.org.uk/html/regulation/html/additives.html

Data Used

Internal Industry Documents

Internal Industry Documents plus statements from J. E. Henningfield, W. A. Farone, etc.

Hypotheses Regarding Ammonia Compounds

- "The Marlboro has maintained a high pH [in smoke] by using a combination of relatively low sugar and ammonium phosphate additive on the reconstituted tobacco." RJR 1973: 51774431 - 51774446
- "The market leaders [Kool and Marlboro] appear to have higher pH's, and hence the higher concentration of free base nicotine." Lorillard 1976: 81091200-81091216
- "A third thing that ammonia-like compounds can do is increase the pH, increase the amount of free-base nicotine, or what Dr. Rickert referred to as unprotonated nicotine.... The free-based form of cocaine or the free-based form of nicotine is more rapidly absorbed, has a more explosive effect on the nervous system. Ammonia is one of the ways that you can provide free-based cocaine or free-based nicotine." J. E. Henningfield 1/30/97
- "The perfect example of that is that if you don't take into account the gas phase, if I do something like increase the pH and the smoke drops so that I can put more of the nicotine from the liquid into the gas and I am not measuring the gas, then in fact, you don't measure that nicotine which gets in the gas phase. This has been known since the late 1960's and early 1970's." W.A. Farone 6/12/97

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Summary of Scientific Data

- Soluble ammonia levels in cigarette filler do not influence ammonia in smoke delivery, nicotine in smoke delivery, or measured "smoke pH." Rickert, 1997; Ellis, et al., 1999
- The majority of nicotine inhaled in cigarette smoke (>90%, irrespective of cigarette type) is retained within the respiratory system. Therefore, the influence of any cigarette design differences on total nicotine retention within the respiratory system is minimal. Dixon, 1999
- The site of nicotine absorption (upper vs. lower) within the respiratory system can influence the rate of nicotine uptake. Russell, et al., 1987; Bergstrom, et al., 1995; Lunell, et al., 1996
- Peak nicotine concentrations seconds after [smoke] inhalation or intravenous injection are much lower than expected. Rose et al., 1999
- Soluble ammonia levels in cigarette filler do not influence the amount of nicotine collected on the Cambridge pad (99.9% collected). Bevan, 1995; Ellis, et al., 1999

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Pankow July 24, 2003 Chem. Res. Toxicol. Article

- Study generated data that were used to calculate an effective value for pH of the smoke.
- Eleven commercial cigarettes investigated.
- Smoking conditions
 - Two cigarettes smoked simultaneously
 - 45 ml puff, 2 second puff duration, 30 sec puff frequency
 - Smoke collected in a 450 ml Teflon bags
 - Puffs 1-3 collected in bag 1 and puffs 4-~11 in bag 2
- Sample analyses
 - After ~ 15 min, a gas sample was withdrawn from the bags and the amount of nicotine determined – this value was used to calculate the amount of “free nicotine.”
 - Ammonia gas was then added to the bags and the analysis of nicotine repeated – this value was used to calculate the amount of protonated nicotine.

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Pankow July 24, 2003 Chem. Res. Toxicol.

Article - Takeaways

- No new hypotheses on ammonia and nicotine.
- Higher values reported for “free nicotine” than previously considered typical for cigarettes.
- Marlboro (KS, HP, filter) reported to have ~ 10% “free nicotine” in first three puffs (effective pH of 7.08) and 3% in latter puffs (effective pH of 6.3).
- Suggests that partially blocking ventilation holes during smoking increases amount of “free nicotine.”
- Higher values reported for “free nicotine” will influence the rate of nicotine uptake by human smokers.

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Pankow July 24, 2003 Chem. Res. Toxicol., OHSU Press Release - Takeaways

- “Thought to be the most addictive form of nicotine in tobacco smoke, free-base nicotine is found at a wide range of levels in popular brands.”
- “During smoking only the free-base form can volatilize from a particle into the air in the respiratory tract. Gaseous nicotine is known to deposit super-quickly in the lungs. From there, it’s transported rapidly to the brain.”
- “Since scientists have shown that a drug becomes more addictive when it is delivered to the brain more rapidly,” Pankow continued, “free-base nicotine levels in cigarette smoke thus are at the heart of the controversy regarding the tobacco industry’s use of additives like ammonia and urea, as well as blending choices in cigarette design.”

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Next Steps

- Ammonia consensus group – October, 2003
- Question: Does ammonia affect the rate and peak level of nicotine absorption?
 - Arterial blood uptake of nicotine for experimental cigarettes with different ammonia levels and brands in Pankow paper – MCV, Richmond.
 - Arterial blood uptake of nicotine for ammonia added to smoke (vent holes) and to filler – CPI, Frankfurt.
 - Nicotine uptake and transfer time to brain (PET) – Duke University.